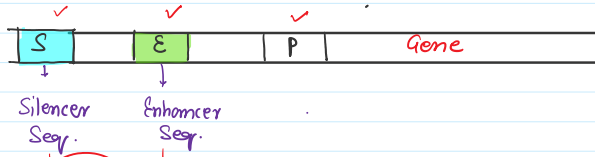


Regulation in Eukaryote

Regulation at Transcriptional level

◦ Initiation level



Regulatory Elements

Cis-acting Elements

✓ Enhancer

Activator

✓ Silencer

Repressor

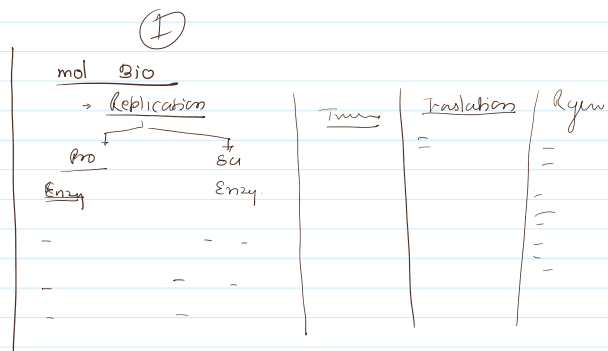
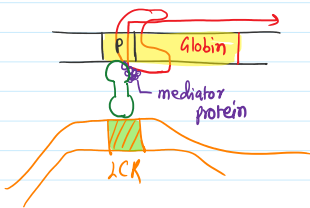
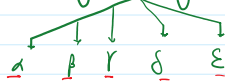
Cis-acting Element → Regulatory Element +nt in
Range of ~ 30 kb near the
gene

Trans acting Element →

eg-

① locus control Region (LCR)

→ involve in Expression of Globin gene

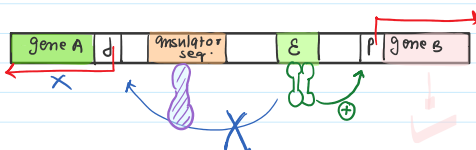


② Global Control Region

Cis-acting Element

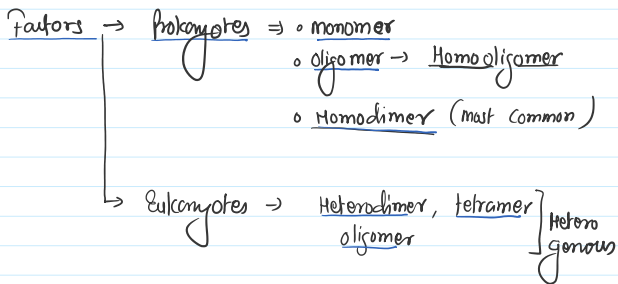
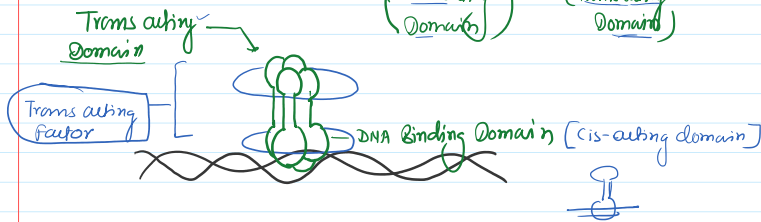
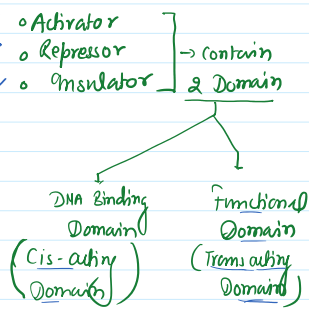
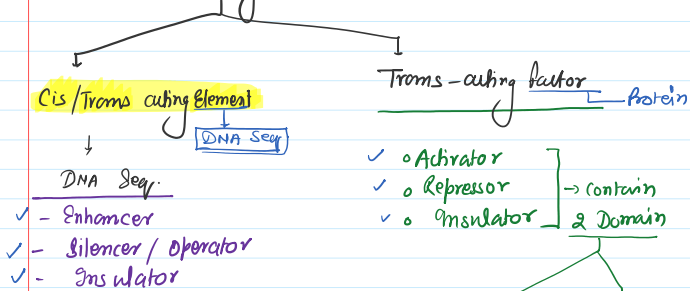
- ✓ Enhancer
- ✓ Silencer
- ✓ Insulator

Enhancer Seq. Can be +nt
toward upstream or down stream
to the gene



Gene Regulation

Gene Regulation



DNA Binding Domain

↳ Super 2° str. k/a motif

① Helix-Turn Helix

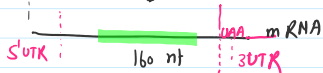
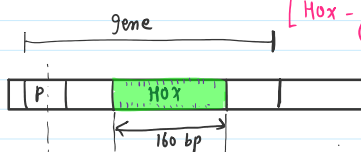


eg. Eukaryotes - Eukaryotic T.F

Contain Homeodomain

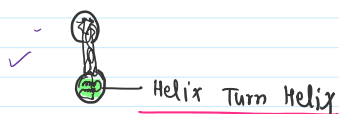
↳ Contain Homeobox gene

[Hox - gene]



ORF

Translation



◦ Conserve a.a seq.

Homeotic gene \rightarrow organ specific gene
 • if mutated \rightarrow change in organ

② Zn-Finger motif

\hookrightarrow most common in Eukaryotes

$C_2H_2 \rightarrow$ contain Zn bridge

eg - T.F. IIIA

- Steroid Hormone Receptor

③ Basic Zipper

\swarrow leucine zipper
 \searrow Helix loop helix

eg - b-zip

eg - myo D

④ AT Hook

- Interacts with AT Rich seq.
- minor groove of DNA

eg - High mobility Group (HMG)

\downarrow
 Chromatin Associated protein

eg - Sox gene

Trans-acting Domain of activator - [Functional Domain]

① Acidic a.a. Containing Domain (Glu, asp rich domain)

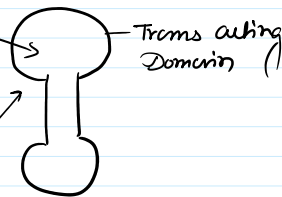
eg - Gal4 & GCN4

② Gln Rich Domain

eg - Sp1

③ Pro-Rich Domain

eg - Fos, Jun, myc



Trans-acting Domain

Activator ✓

Repressor

- ① • Recruitment of basal T.F.

- ② • Recruitment of RNA Pol. Through mediator protein

- Inhibit binding of basal T.F.

- Brings -ve allosteric change

- ② Recruitment of RNA Pol.
Through mediator protein
 - ③ Brings +ve Allosteric change
(Close → open complex)
 - ④ Chromatin Remodelling
Heterochromatin → Euchromatin
- Brings -ve allosteric change
Open → Close
 - Mask activator site
 - Steric Exclusion of RNA Pol.
 - Chromatin Remodelling
 - Euchromatin → Heterochromatin

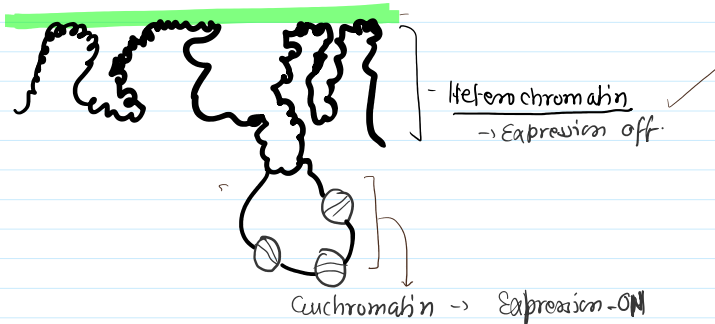
Eukaryotic gene Regulation

- ✓ ① Genomic level of Gene Regulation
- ✓ ② * Transcriptional level of Gene Regulation
- ✓ ③ * Post Transcriptional level Gene n
 - ✓ → Alternative Splicing
 - ✓ → Polyadenylation
 - ✓ → Trans-splicing
 - ✓ → RNA editing
 - ✓ → Small RNA mediated gene silencing

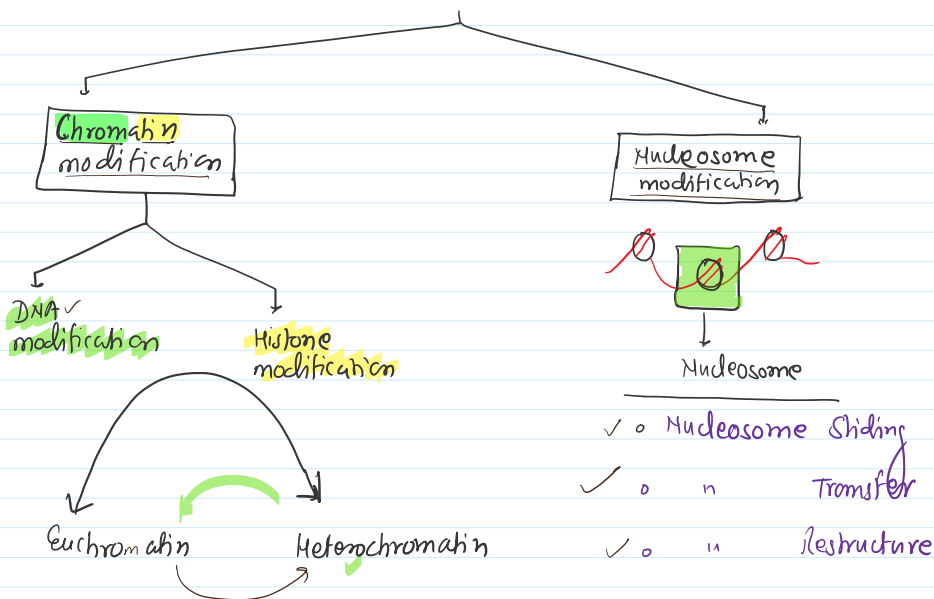
* Translational level gene Regulation

- Initiation ✓
- Post Translational ✓

Genomic level of Gene Regulation



Regulation of Gene Expression at Genomic level



#

① Chromatin modification

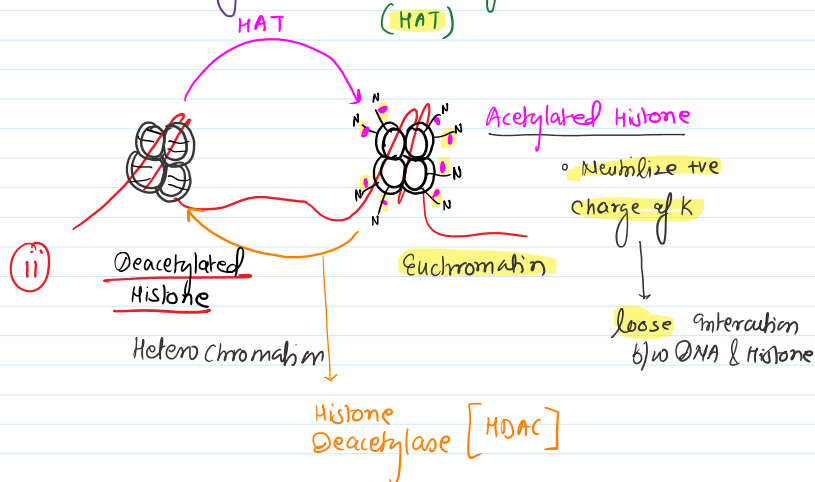
① Histone modification

① Acetylation on Histone

- on K residue toward N-Ter. of Histone

[Rchain of K residue]

- Enzyme - Histone acetyl Transferase (HAT)



- * Acetylated Histone Can recruit Some **activator** That contain **bromodomain**
- ↓
- Expression ↑**

Deacetylation of Histone can be done

by **HDAC** **Chromodomain** **acetylase**

by HDAC

↓

Contain Chromodomain

Chromodomain

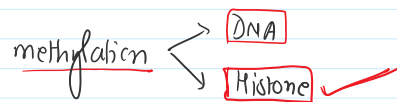
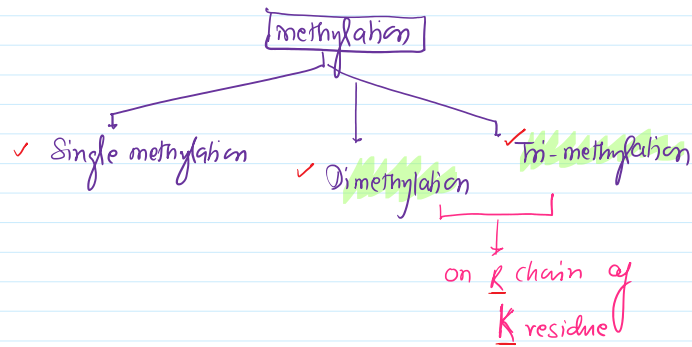
↓

Euchromatin Heterochromatin

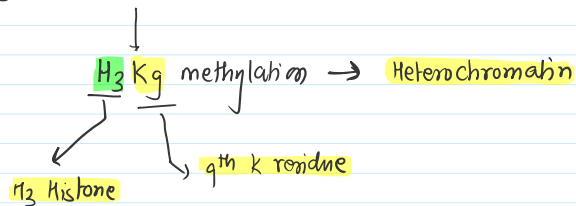
↓

Expression ↓

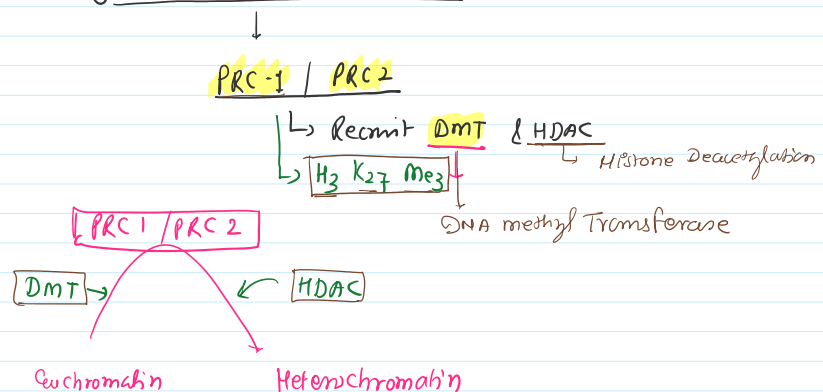
- on k or some times Q

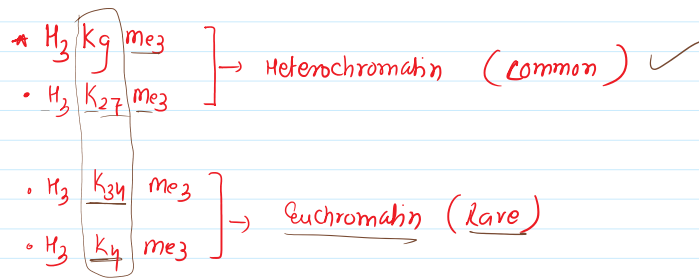


eg- (i) $S_u - (\text{Var}) = 3 - 9$

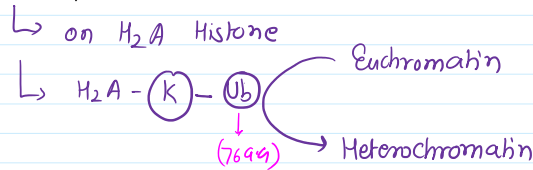


(ii) Polycomb Repressor Complex (PRC)





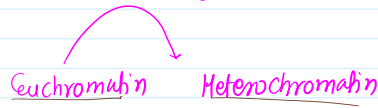
④ Monoubiquitination



④ Sumoylation

Small Ubiquitin like modification

- Small ub like protein (96 a.a.) add on
- chain of K



⑥ Phosphorylation

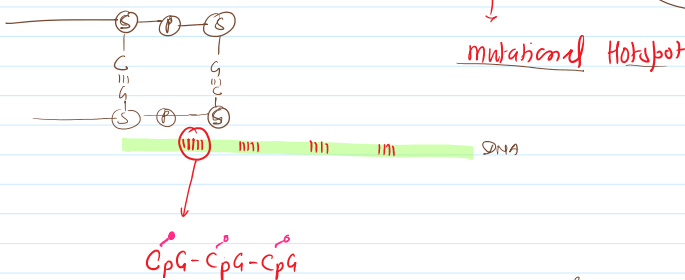
- $H_3 S_{10} - P$
- loose interaction b/w DNA & Histone



DNA modification

- methylation on gene for \rightarrow gene silencing
- site for methylation = CpG island

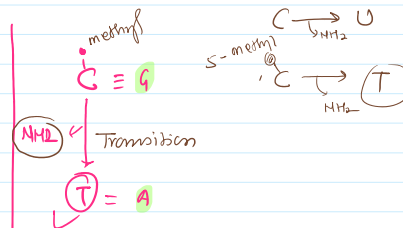
most common site



5 methyl - Cytosine

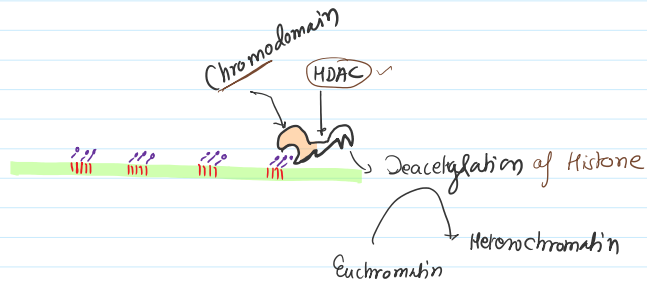
deamination

Thymine (5 methyl uracil)



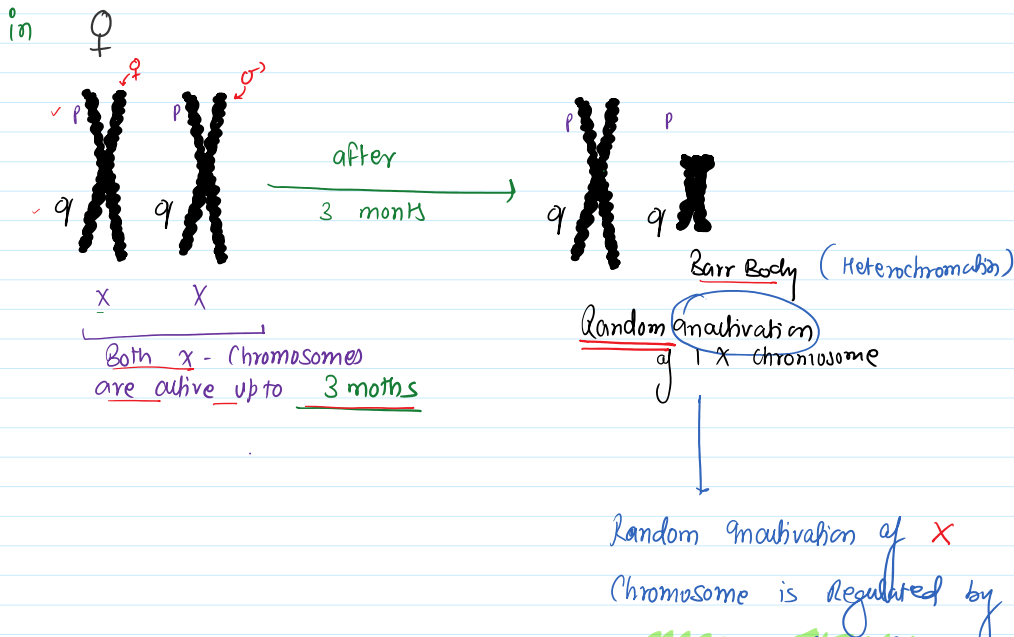
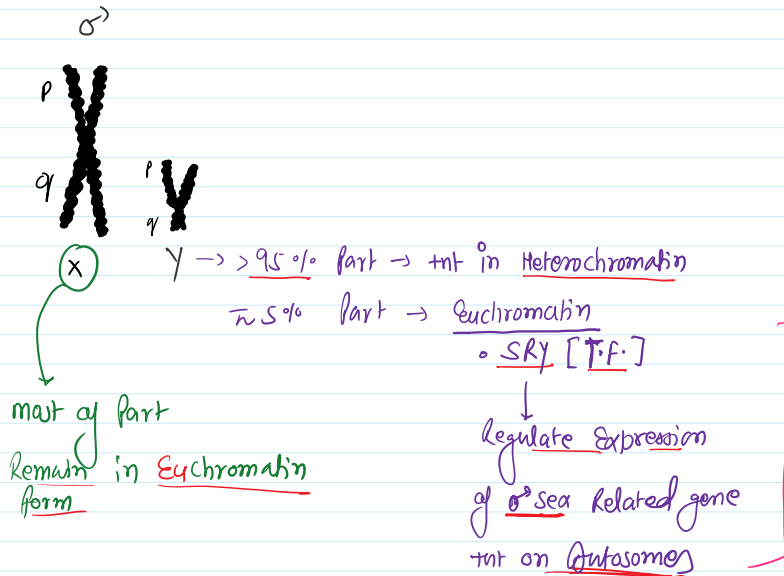
Thymine (5 methyl Uracl)

T = A

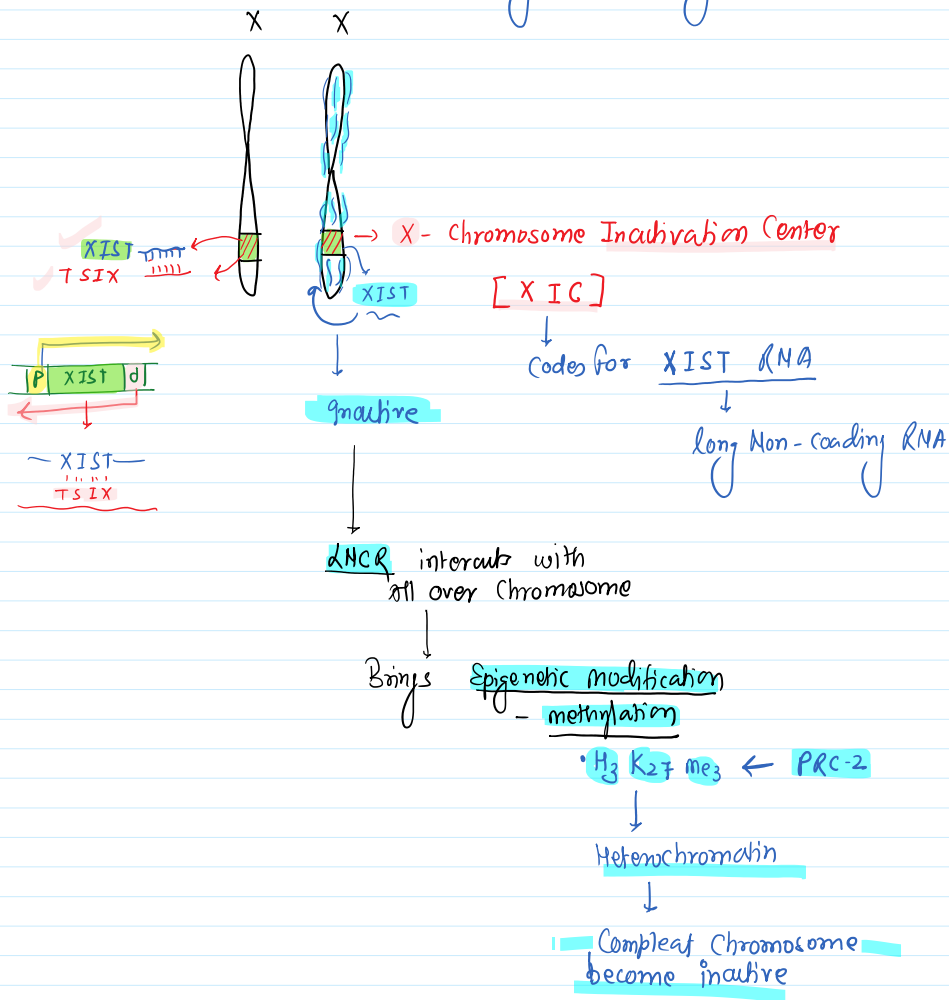


eg - Dosage Compensation

→ Random inactivation of X-Chromosome
/ Lyonization / Barr Body formation



Chromosome is regulated by
a Long Non-Coding RNA



Q = XXX in a female
↓
2 Barrbody

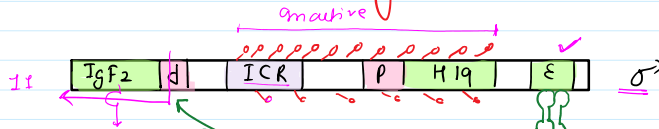
✓ 2nd eq - - Genome Imprinting

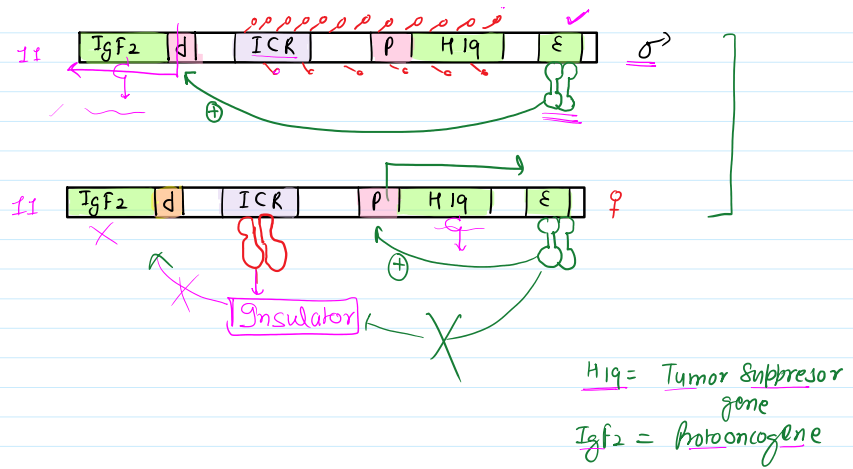
- Epigenetic modification
- No change in gene seq.
- But change in Expression Pattern

may follow Generation after Generation

eg. ① → Chromosome No. 11 (Human)

↓ Genome imprinting

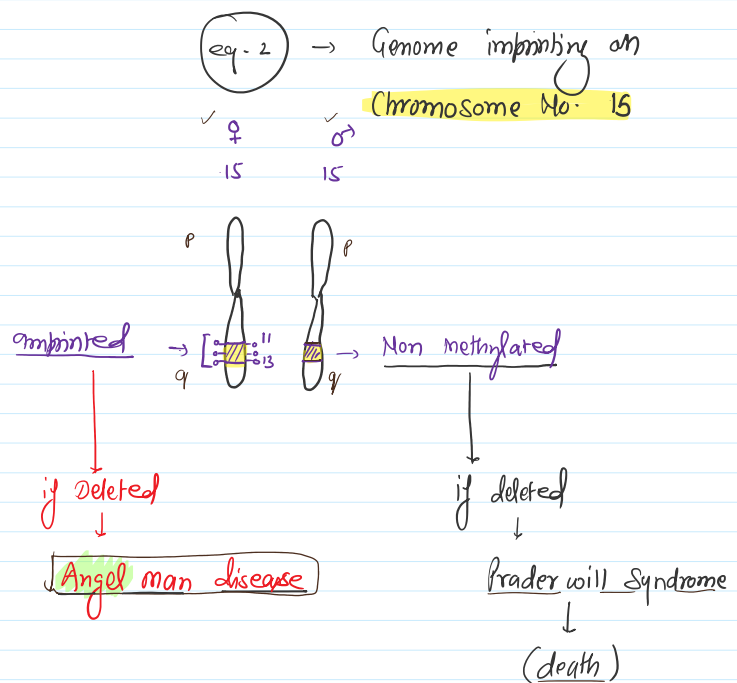




if IgF2 Expression \uparrow = $\frac{\text{insulin}}{\downarrow}$ \uparrow = Growth uncontrolled \rightarrow Tumor \downarrow Cancer

Back with Wiedemann disease

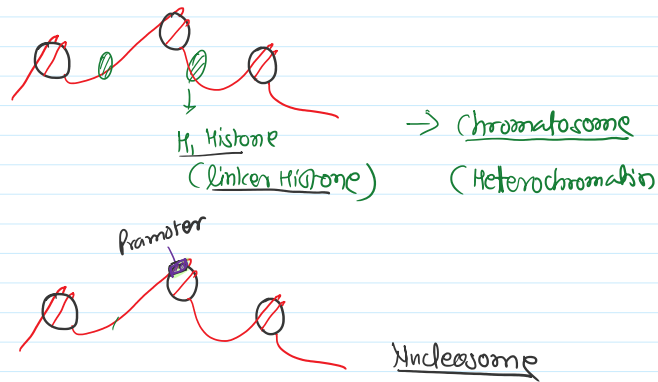
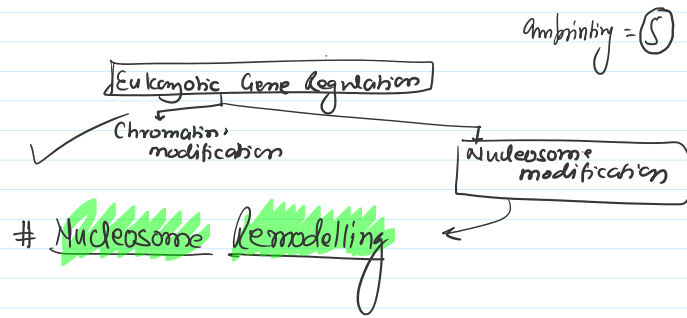
if H19 Expression \uparrow = Stunted growth observed



Q# gene A \rightarrow mice \rightarrow Transgenic mice \rightarrow 1st gen. \rightarrow All \rightarrow No Expression

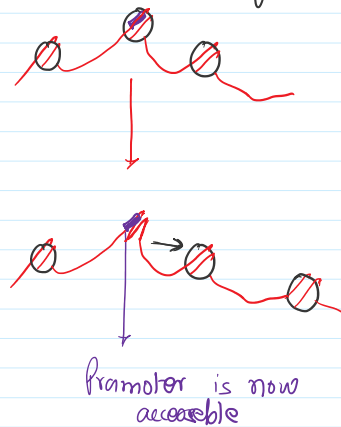
1st gen. \rightarrow All \rightarrow Expression observed

imprinting = 5



3 processes by which
gene expression occurs in Nucleosome str.
(when Promoter is occupied by Histone)

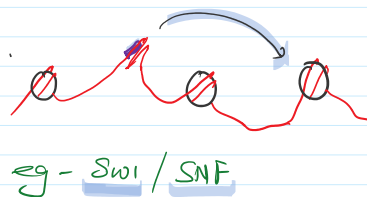
① Nucleosome Sliding



eg Swi/SNF

↳ Recruit Bromodomain protein
↳ Promote Nucleosome Sliding

② Nucleosome Transfer



③ Nucleosome Restructure



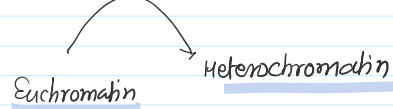
eg - Swi/SNF (Bromodomain)

- ↳ ATP dependent ✓
- ↳ formation of Euchromatin ✓
- ↳ Gene Expression ↑ ✓

* Initiator of Switch (ISwi)

- ↳ Sliding (ATP Dependent) ✓
- ↳ Recruit Bromodomain ✓
- ↳ Gene Expression ↑ ✓

• NuRD/CHD → Sliding
↳ Recruit Chromodomain

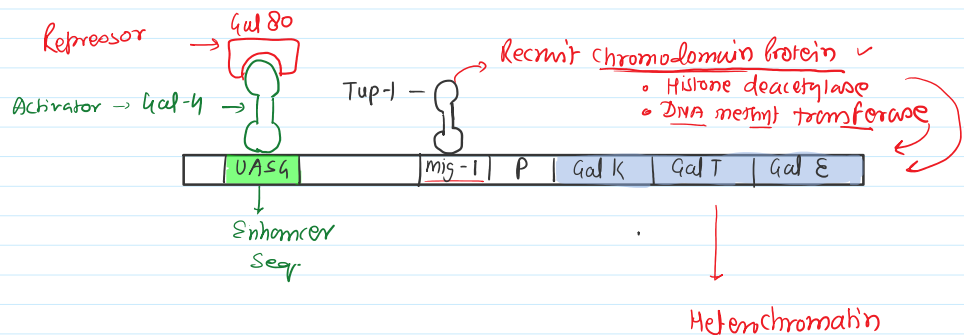


- ATP Dependent
- Gene Expression ↓

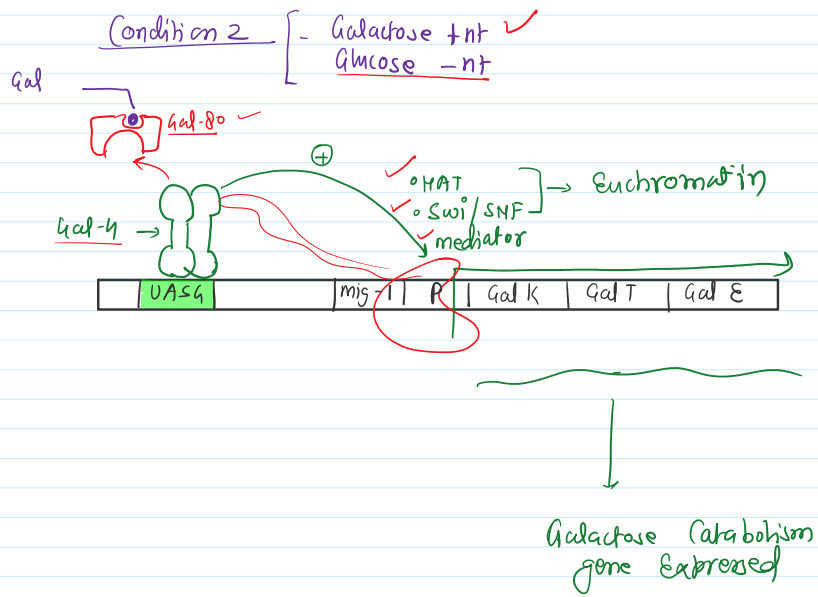
Regulation of Gene Expression at Transcriptional Initiation level

eg - Gal operon (gmp)

Condition 1 [Glucose +nt
Galactose -nt] → operon off

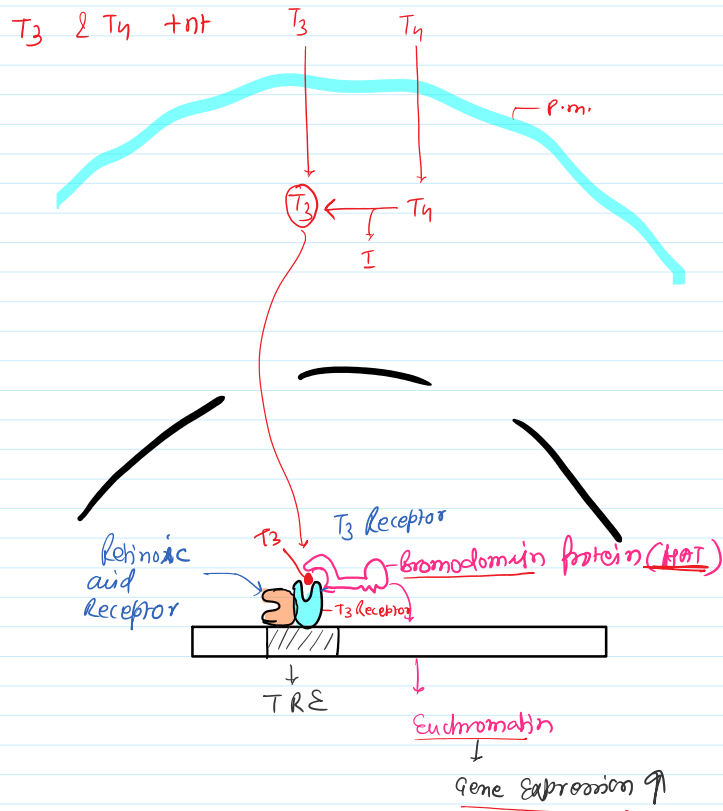


Condition 2 [- Galactose +nt ✓
Glucose -nt]



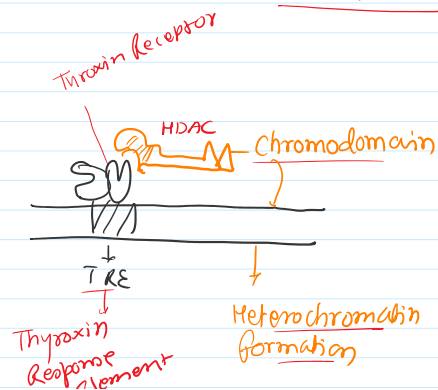
Regulation by T₃ Hormone (Thyroxine)

✓ Condition - 1

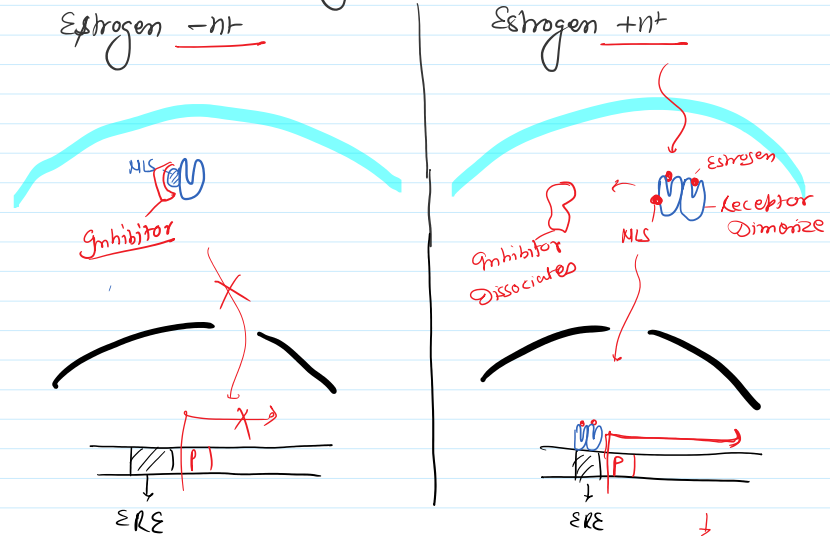


Condition 2

T₃ & T₄ ↓



Gene Regulation Estrogen



Post Transcriptional Gene Regulation

* Alternative Splicing →

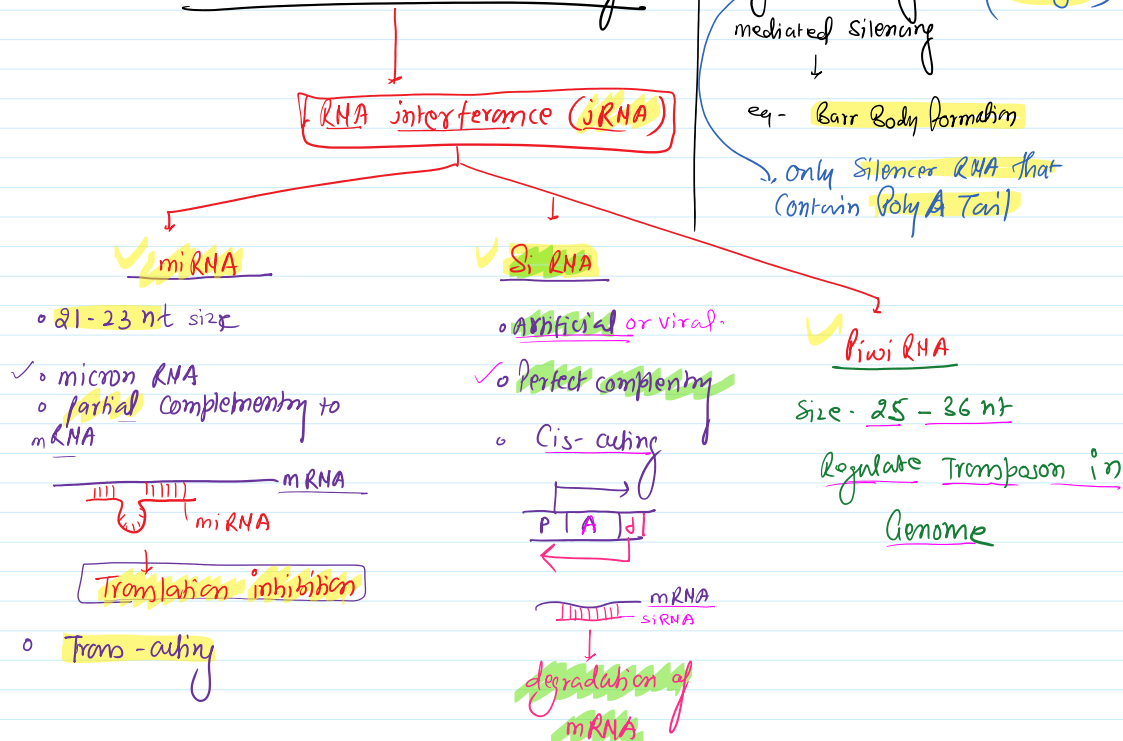
- T-Antigen
- Sex determination

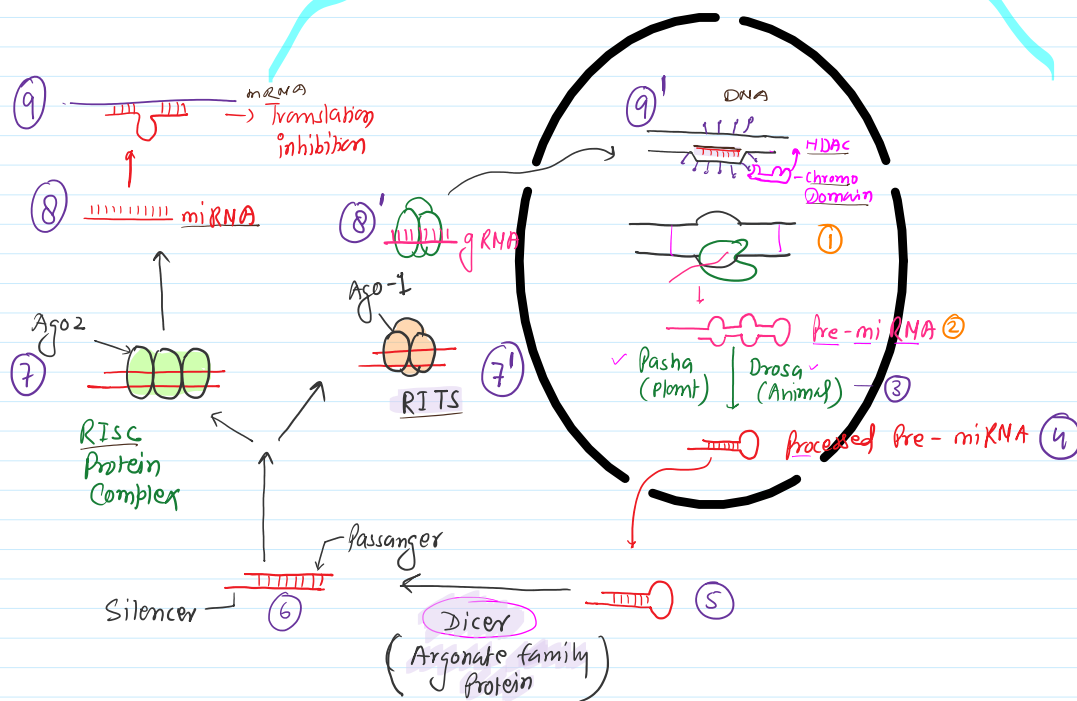
• Alternative Polyadenylation - B-cell (Ab Secretion)

• Trans-splicing - Trypanosoma

• RNA Editing - Apolipoprotein

Small RNA mediated Silencing





Dicer Recognize DS RNA & processed it

RISC → RNA Induced Silencing Complex

RITS → RNA n Transcription Silencing

Regulation at Translational level

Global Regulation

◦ Global Translational Inhibition